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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,548	01/16/2004	Peter Rogowsky	A36125PCT USA-A	8731

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EXAMINER	
WORLEY, CATHY KINGDON	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 08/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/759,548	ROGOWSKY ET AL.	
	Examiner	Art Unit	
	Cathy K. Worley	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *3,5,12-14 and 35-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-11 and 15-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/3/04+*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction/Election

1. In response to the communications received on May 19, 2006 and Feb. 23, 2006 from Lisa B. Kole, the election with traverse of group I, claims 1-11 and 15-34 as they relate to SEQ ID NOs: 1, 3, and 5, is acknowledged. Claims 3 and 5 are drawn to non-elected sequences, and therefore they are withdrawn from consideration. The Applicant specifically traverses the restriction between groups I and II (see page 4 of response received on Feb. 23, 2006). The Applicant argues that a search for the polynucleotides of group I will encompass the primers of group II (see page 4 of response). This is not persuasive, however, because the claims of group I (for example claim 1) are not commensurate in scope with the claims of group II (for example claim 12). Therefore, a search for the polynucleotides of group I will not cover the primers of group II, and the restriction between the groups is proper. The restriction requirement is MADE FINAL. Claims 1-41 are pending, claims 3, 5, 12-14, and 35-41 are withdrawn from consideration. Applicant is advised to amend the claims to read on the elected invention only.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on July 18, 2001. It is noted, however, that applicant has not filed a certified copy of the French application (FR 01/09,631) as required by

35 U.S.C. 119(b). Therefore, the instant application does not get the benefit of the July 18, 2001 priority date.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: - - Nucleic acids encoding a maize chloroplast L35 protein and causing altered germ development - - .

4. The abstract of the disclosure is objected to because it is not sufficiently descriptive of the invention. The abstract should be between 50-150 words in length and it should specify that the nucleic acids encode the maize chloroplast L35 protein. Support for this language can be found on page 73 in paragraph 00297. Correction is required. See MPEP § 608.01(b).

5. The use of the following trademarks has been noted in this application: EPPENDORF and HYBOND N. They should be written in all capital letters wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

6. The specification is objected to because it contains an embedded hyperlink and/or other forms of browser-executable code. On page 100 in paragraph 00393

there is an embedded link. Applicant is required to delete the embedded hyperlinks and/or other forms of browser-executable code. See MPEP 608.01.

Information Disclosure Statement

7. The listing of references in the specification on pages 105-111 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 18 and 19 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 7-11, 18-19, 21, 26, 28-30, and 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in this rejection.

The term "overexpression" in claim 7 is a relative term which renders the claim indefinite. The term "overexpression" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Does this mean double the expression of the endogenous gene in a wild type plant? Does this mean expression in a different temporal or spatial pattern than the endogenous gene in a wild-type plant? The metes and bounds of this claim are unclear.

The term "sensitive" in claim 8 is a relative term which renders the claim indefinite. The term "sensitive" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 11 recites the limitation "the inducible activator" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Claim 11 also recites the limitation "the GVG activator" in lines 2-3 and the limitation "the rice actin 1 gene promoter" in lines 3-4. There is insufficient antecendent basis for these limitations in the claim.

Claims 18 and 19 provide for the use of the nucleic acid of claim 1 or claim 6, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

The term "rich in oil" in claim 19 is a relative term which renders the claim indefinite. The term "rich in oil" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

10. Claims 1-4, 6-11, and 15-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 6-11, and 15-34 are drawn to nucleic acids, vectors, host cells, plants, and methods comprising a polynucleotide encoding a polypeptide with at

least 95% identity to SEQ ID NO:5 or a polynucleotide encoding a polypeptide comprising at least 100 consecutive amino acids of SEQ ID NO:5, or a complement thereof.

The proposed function of these nucleic acids is to inhibit expression of the endogenous gene (see page 64 paragraph 00260) or to overexpress the gene (see page 12 paragraph 0058). The specification teaches that a mutant plant that has an insertion in the endogenous gene produces grains consisting essentially of the albumen (see page 11 paragraph 0055) which is useful for industrial processing (see page 3 paragraph 0009). The disclosure speculates that transgenic plants engineered to inhibit expression of the endogenous gene will have a similar phenotype and could be used by the agrofoods industry, the pharmaceutical industry, or the paper industry (see page 68 paragraph 00275 and page 70 paragraph 00284). The disclosure further speculates that transgenic plants engineered to overexpress the gene will have seeds or grains enriched in oil (see page 63 paragraph 00256). Therefore, the essential feature of the instant nucleic acids is that they are either effective for inhibiting expression of the endogenous gene, or that they encode a functional protein.

The amino acid sequence of SEQ ID NO:5 is disclosed to be that of a chloroplast L35 protein (see page 73, paragraph 00297) which is a member of the 50S ribosome from the maize chloroplast (evidenced by Magnard et al. (2004) Plant Physiology, Vol. 134, pp. 649-663). The instant application has described the full-

length L35 protein by disclosing SEQ ID NO:5, but the instant application has not described any proteins having 95% identity to SEQ ID NO:5. SEQ ID NO:5 consists of 143 amino acids, therefore, a protein having 95% identity will have 7 substituted amino acid residues. Given that there are 19 different amino acids that could be present for each of these substitutions, this encompasses 19^{143} molecules for each substitution. Furthermore, the claims encompass fragments with only 100 amino acids, and there are 990 different possible molecules that comprise at least 100 contiguous amino acids of SEQ ID NO:5. The specification has not provided disclosed which domains, motifs, or subsequences are required for proper function of the L35 protein, and therefore, one would not know what structures (sequences) are required for this function.

With regard to inhibition of expression, the claims encompass the same large genus of molecules by reciting "complements thereof". The claims are directed to nucleic acids encoding this large genus of polypeptides, and due to codon degeneracy, this will encompass approximately 3 times that number of polynucleotides (3×19^{143}).

Given the breadth of the claims encompassing multitudes of molecules with not even one embodiment reduced to practice, and given the lack of description correlating structure and function, the written description requirement has not been met.

11. Claims 1-4, 6-11, and 15-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-4, 6-11, and 15-34 are broadly drawn to nucleic acids, vectors, host cells, plants, and methods comprising a polynucleotide encoding a polypeptide with at least 95% identity to SEQ ID NO:5 or a polynucleotide encoding a polypeptide comprising at least 100 consecutive amino acids of SEQ ID NO:5, or a complement thereof.

The nature of the invention is a molecular biological approach to engineer transgenic plants to either phenocopy insertional mutants or to possess an opposite phenotype compared to the insertional mutants (see discussion above).

The instant specification fails to provide even one working example. The proposed phenotypes of the plants are prophetic. Whether or not an insertional mutant can be mimicked by using anti-sense to suppress the endogenous gene is highly unpredictable, because there is no guarantee that antisense will result in a 100% knockout such as that of the insertional mutant.

In addition, the claims encompass the use of antisense in multiple plant species. Antisense suppression of gene expression is highly unpredictable, and the prior art suggests that success depends on the percent identity between the

sequence of the antisense construct and the target gene sequence (see Elomaa et al. (1996) Molecular Breeding, Vol. 2, pp. 41-50; paragraph bridging pages 47-48, in particular). In the prior art, Klee et al. teach that antisense genes would probably be species-specific, and therefore a different antisense gene would be required for each species of plant desired to be transformed (see US Patent # 5,702,933, issued Dec. 30, 1997, column 1 lines 60-65, in particular).

Magnard et al. teach that the L35 gene is a member of a gene family (see page 653, Figure 4A). In another study, Colliver et al. taught that antisense of members of a gene family is highly unpredictable (PMB (1997) Vol. 35, pp. 509-522). Colliver et al. showed that transformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase resulted in transformants with increased levels of chalcone synthase transcripts due to increased transcription of other members of the gene family (see page 519 left column paragraph 2, in particular).

Because of the sequence variability between the different genes in different species of plants and because of the inconsistent results taught in the prior art, there is a high degree of unpredictability in the use of antisense to inhibit the expression of different genes. Given the lack of even on working example, and a high degree of unpredictability as discussed above, it would require undue experimentation on the part of one of skill in the art to make and use the invention as claimed.

With regard to the claims for overexpressing SEQ ID NO:5, the instant application has not provided even one working example. The proposed phenotype is prophetic. The polypeptide of SEQ ID NO:5 is a member of a large multimeric complex, the 50S ribosomes in plastids (see Magnard, page 653, paragraph bridging left and right columns). The polypeptide of SEQ ID NO:5 has no known function by itself. Unless all of the other polypeptides in the 50S ribosome are overexpressed in stoichiometric quantities, one would not expect to have any phenotype at all. Therefore, it would require undue experimentation on the part of one of skill in the art to use the invention as claimed.

The Applicant is invited to submit evidence in the form of a declaration to show that they have produced a plant using the nucleic acids and methods taught in the instant specification, and that the plants have the proposed phenotypes. In the even that such a declaration is filed, the claims would be limited in scope to the precise nucleic acids, method steps, and plants utilized, due to the unpredictability discussed below.

As discussed above in the written description requirement, the claims encompass a large genus of molecules. The instant specification fails to provide guidance for which amino acids of SEQ ID NO:5 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain the functional activity of the encoded protein. The specification also fails to provide

guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional L35 ribosomal protein.

Making substitutions in proteins does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would have at least 95% identity to the original protein. The nucleic acids encoding all these mutated proteins, however, would hybridize under high stringency to the nucleic acids encoding the original protein.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids encoding over 1 billion proteins with at least 95% identity to SEQ ID NO:5. Making all possible single amino acid substitutions in an 143 amino acid long protein like that encoded by SEQ ID NO:5 would require

making and analyzing 19^{143} nucleic acids; these proteins would have 95% identity to SEQ ID NO:5. Because nucleic acids encoding proteins with 95% identity to SEQ ID NO:5 would encode proteins with 7 amino acid substitutions, many more than 19^{143} nucleic acids would need to be made and analyzed. Guo et al (2004, Proc. Natl. Acad. Sci. USA 101: 9205-9210) teach that while proteins are fairly tolerant to mutations resulting in single amino acid changes, increasing the number of substitutions additively increases the probability that the protein will be inactivated (pg 9209, right column, paragraph 2). Thus, making and analyzing proteins with 7 amino acid substitutions that also are functional L35 ribosomal proteins would require undue experimentation.

Claim Rejections - 35 USC § 102

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Wen et al. (GenBank Accession AI374506, published on Jan. 21, 1999).

Claims 2 and 4 are drawn to a nucleic acid comprising at least 300 contiguous nucleotides of SEQ ID NOs: 1 or 3.

The nucleic acid sequence taught by Wen et al. has over 300 contiguous nucleotides of SEQ ID NO:1 beginning at position 3645 of SEQ ID NO:1 (see sequence alignment). The nucleic acid sequence taught by Wen et al. has over 300

contiguous nucleotides of SEQ ID NO:3 beginning at position 241 of SEQ ID NO:3 (see sequence alignment).

13. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Walbot, V. (GenBank Accession BI233829, published on July 11, 2001).

Claim 1 is drawn to a nucleic acid encoding at least 100 contiguous amino acids of SEQ ID NO:5.

Walbot teaches a nucleic acid encoding a polypeptide with over 100 contiguous amino acids of SEQ ID NO:5 beginning with position 9 of SEQ ID NO:5 (see sequence alignment).

14. Claims 26 and 32-34 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Neuhaus et al. (WO 99/58654, published on Nov. 18, 1999).

A rejection under 35 U.S.C. 102 or 103 does not require the same analysis as a rejection under 35 U.S.C. 102 or a rejection under 35 U.S.C. 103. The rejection is made because the Examiner cannot determine whether the prior art plant possesses characteristics that are not recited in the art. The Examiner does not have sufficient facts to determine whether the claimed plants and seed products are inherently the same as the prior art plants and seed products. In addition, the Examiner cannot conclude that the claimed subject matter would have been obvious since it cannot be determined whether the claimed and prior art plants differ. Where the prior art product seems to be identical, except that the prior art is silent

to a characteristic or property claimed, then the burden shifts to Applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. See *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Claims 26 and 32-34 are drawn to a hybrid transgenic plant, a product of the seed produced by the claimed method, and starch and meal or oil from the seed produced by the claimed method.

Neuhaus et al. teach a hybrid transgenic plant (see page 14, second paragraph). They also teach starch and oil (see abstract and claims 8 and 11). Because the hybrid plant of claim 26 is produced by crossing a plant that can be heterozygous for the transgene, the resulting hybrid plant need not comprise the nucleic acid of the instant invention. If the plant claimed in the instant claim 25 were crossed with the plants taught by Neuhaus et al., 50% of the resulting hybrid transgenic plants would be indistinguishable from the hybrid taught by Neuhaus et al. With regards to the oil and starch (which are products of the seeds), Neuhaus et al. teach oil and starch from their plants (see abstract and claims 8 and 11). Oil and starch do not contain DNA, and therefore, the oil and starch from a wild-type plant or a different transgenic line are indistinguishable from the oil and starch of the instant claims. (See MPEP § 2113 for information on Product by Process claims.)

15. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Walbot, V. (GenBank Accession BI358791, published on July 31, 2001).

Claim 1 is drawn to a nucleic acid encoding a polypeptide with at least 100 contiguous amino acids of SEQ ID NO:5.

Walbot teaches a nucleic acid encoding the entire polypeptide of SEQ ID NO:5 with 100% identity (see sequence alignment).

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CKW
July 27, 2006

ANNE KUBELIK, PH.D.
PRIMARY EXAMINER